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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,283	07/08/2003	Tsu-An Hsu	8842.0002	2562

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EXAMINER	
GARVEY, TARA L	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,283	HSU ET AL.	
	Examiner	Art Unit	
	Tara L. Garvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *19,20,25,31 and 33-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18, 21-24, 26-30 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-41 are pending.

Election/Restrictions

Claims 19, 20, 25, 31 and 33-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 18, 2005.

Applicant's election with traverse of Group I (claims 1-18, 21-24, 26-30 and 32) in the reply filed on August 18, 2005 is acknowledged. The traversal is on the ground(s) that the inventions are not distinct and a search burden does not exist because a search for the expression vector of Group I will overlap a search of the other groups. This is not found persuasive because the inventions are distinct and a search burden exists. While searches may partially overlap, they also extend beyond one another. In, for example, the case of a product and a process of using that product, a reference may exist that teaches the product of Group I drawn to dicistronic expression vectors, but does not teach the same method of using this product as claimed in Group V, which is drawn to a method of treating a patient using the expression vectors.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Claims 1-18, 21-24, 26-30 and 32 are granted priority to the filing date of July 8, 2003 for the instant application since reference to the priority applications does not appear in the first paragraph of the specification. Once the claim to the priority application appears in the specification, claims 1-18, 21-24, 26-30 and 32 will be granted priority to provisional application with a filing date of July 9, 2002.

If applicant desires benefit of a previously filed application under 35 U.S.C. 119 (e), specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence(s) of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an

international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Information Disclosure Statement

The information disclosure statement received on September 27, 2003 has been considered. Application 10/614,202 was considered, but the citation was changed to the patent application publication number since this is a published document.

Claim Objections

Claim 30 is objected to because of the following informalities: In line 1 of part (b), "or" should be "of". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18, 21-24, 26-30 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not describe all the variants or fragments of an IRES from EV71, HCV or EMCV that would function as an IRES in the expression vectors and recombinant viruses of the claimed invention. The specification simply defines a 'fragment' as a portion of the IRES and a 'variant' as the IRES with a different

nucleotides sequence due to nucleotide substitutions, deletions or additions that maintain the function of the IRES without providing any specific examples. The prior art does not offset the lack of description in the specification in that it does not describe all the variants or fragments of the IRES from EV71, HCV or EMCV that are able to maintain the function of the IRES in the expression vectors and recombinant viruses. Therefore, there is not a structural and functional relationship provided by the prior art or the specification for one of skill in the art to envision all the variant structures of an IRES from EV71, HCV or EMCV posses the same function as the full length IRES from these viruses.

Claims 6-10, 15-18, 27-30 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not describe all the homologs of an IRES from EV71, HCV or EMCV that would function as an IRES in the expression vectors and recombinant viruses of the claimed invention. The specification simply defines a 'homolog' as "structure or processes in a different organisms that show a fundamental similarity" without describing any specific homologs. The prior art does not offset the lack of description in the specification in that it does not describe all the homologs of the IRES from EV71, HCV or EMCV that are able to maintain the function of the IRES in the

expression vectors and recombinant viruses. Therefore, there is not a structural and functional relationship provided by the prior art or the specification for one of skill in the art to envision all the structures that are homologs of an IRES from EV71, HCV or EMCV and posses the same function as an IRES from these viruses.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6, 21, 24, 27 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The metes and bounds of the claimed subject matter are not defined. The phrase "a variant or fragment thereof" does not define the scope of the limitations.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Urabe et al (Gene (1997) volume 200, pages 157-162).

Claims 1-5, 11 and 13 are drawn to a nucleic acid vector and a biological vector that comprise a promoter operably linked to at least two cistrons which can be either a reporter gene or a therapeutic gene and a nucleotide sequence for an IRES from EV71, HCV or EMCV that is operably linked to at least one of the cistrons and to host cells containing the vectors.

Urabe et al teaches a dicistronic adeno-associated vector (AAV) that comprises a CMV promoter, either a reporter gene such as luciferase or a therapeutic gene, the HCV-IRES or EMCV-IRES and a selectable marker gene and mammalian 293 cells that contain the constructs (abstract, page 158, left column last paragraph, Figure 1 and right column bridging page 159, left column, page 159, right column, first full paragraph bridging page 160, left column, line 1, page 160, right column, second and third full paragraphs, page 161, left column, first paragraph and right column, first full paragraph). Thus, Urabe et al teach all that is recited in the instant claims.

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by van Zonneveld et al (US 6,447,768).

Claims 1, 3-5, 11 and 13 have been described previously.

van Zonneveld et al teaches a dicistronic adenoviral vector that comprises a CMV promoter, NO synthase cDNA, IRES from EMCV and VEGF 121 or FGF4 cDNA as the angiogenic factors and cells containing the adenoviral vector (abstract, column 5,

lines 40-67 bridging column 6, lines 1-34 and column 18, lines 15-57). Thus, van Zonneveld teaches all that is recited in the instant claims.

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Whitley et al et al (US 6,764,675).

Claims 1, 3-5, 11 and 13 have been described previously.

Whitely et al teaches a dicistronic herpes simplex virus (HSV) vector that comprises an Egr-1 promoter, the p40 and p35 subunits of mIL-12 separated by an IRES from EMCV and mammalian cells containing the vector (abstract, column 5, lines 10-21, column 6, lines 40-67 bridging column 7, lines 1-59 and column 8, lines 48-67 bridging column 9, lines 1-31). Thus, Whitley et al teaches all that is recited in the instant claims.

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Agarwal et al (US 6,194,212)

Claims 1-5, 11 and 13 have been described previously.

Agarwal et al teaches a dicistronic retroviral vector comprising a retroviral promoter such as LTR and an IRES from EMCV separating the RevM10 gene and the marker gene Lyt-2 and cells containing the retroviral vector (column 2, lines 62-67 bridging column 3, lines 14-43, column 4, lines 7-23 and column 7, lines 34-67 bridging column 8 lines 1-53). Thus, Agarwal et al teach all that is recited by the instant claims.

Claims 1, 3-5, 11 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Seguela et al (US 2003/0219858)

Claims 1, 3 and 11 have been described previously. Claim 14 limits the vector to being contained in a bacterial cell.

Seguela et al teaches a bicistronic nucleic acid vector that comprises a CMV promoter and two nucleic acid sequences encoding ASIC2A and ASIC3 polypeptides separated by an IRES from EMCV and E. coli cells containing the vector (page 18, right column, paragraph [0186]). Thus, Seguela et al teaches all that is recited in the instant claims.

Claims 1, 2, 4, 5, 11, 12, 21, 22, 24 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Finkelstein et al (Journal of Biotechnology (1999) volume 75, pages 33-44 referenced in the IDS submitted on September 27, 2004).

Claims 1, 2, 4, 5 and 11 have been described previously. Claim 12 limits the host cell containing the biological vector to an insect cell. Claims 21, 22, 24 and 26 are drawn to a baculovirus transfer vector and a recombinant baculovirus for the expression of two cistrons comprising a baculovirus promoter and an IRES that provides IRES activity.

Finkelstein et al teaches a bicistronic baculovirus vector that comprises the baculovirus polyhedrin promoter (Ppol) and an EMCV IRES separating two reporter genes such as chloramphenicol transferase (CAT) and firefly luciferase (LUC) and recombinant baculoviruses (abstract, page 34, right column, first full paragraph, page

35, left column, last paragraph bridging right column, page page 36, Figure 1 and page 37, Figure 2 and right column, last paragraph bridging page 38, left column). The vector would inherently have IRES activity since the EMCV IRES is known to have IRES activity. The EMCV IRES contained within the baculovirus vector and recombinant baculovirus is capable of having IRES activity in a mammalian cell (page 38, left column, first full paragraph, lines 28-30 and right column, lines 13-16). Furthermore, Finkelstein et al teach the baculovirus vector and the recombinant baculovirus contained in host cells such as different species of insect cells and demonstrate that the EMCV IRES has residual IRES activity in these cells (page 43, left column, first full paragraph, lines 20-25). Thus, Finkelstein et al teaches all that is recited in the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urabe et al (Gene (1997) volume 200, pages 157-162) in view of Kirkegaard et al (US 2004/0052765 A1).

Claims 1-5, 11 and 13 have been described previously.

Urabe has been described previously.

Urabe et al does not teach using a poxvirus as the biological vector.

Kirkegaard et al teaches a dicistronic vaccinia virus vector that comprises a poliovirus IRES separating coding sequence for poliovirus 3A and GFP (page 9, left column, paragraph [0091]).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Urabe et al to use a poxvirus as the biological vector for expression of two cistrons. One would have been motivated to do so in order to receive the expected benefit, as suggested by Urabe et al and actually exemplified by Kirkegaard et al, of expressing two cistrons separated by an IRES in a vaccinia virus for expression of a therapeutic gene. Absent of any evidence to the contrary, there would have been reasonable expectation in using a vaccinia virus vector to express two cistrons since these poxvirus vectors have been used previously for dicistronic expression of therapeutic or reporter genes in cells.

Claims 1-5, 11-13, 21- 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urabe et al (Gene (1997) volume 200, pages 157-162) in view of Kirkegaard et al (US 2004/0052765 A1).

Claims 1-5, 11-13, 21- 24 and 26 have been described previously.

Finkelstein et al has been described previously.

Finkelstein et al does not teach using the HCV IRES in the dicistronic baculovirus vector or recombinant containing a therapeutic gene.

Urabe et al teaches using either an HCV IRES or and EMCV IRES in a dicistronic AAV vector that contains a therapeutic gene (abstract, page 158, left column last paragraph, Figure 1 and right column bridging page 159, left column, page 159, right column, first full paragraph bridging page 160, left column, line 1, page 160, right column, second and third full paragraphs, page 161, left column, first paragraph and right column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the teachings of Finkelstein et al to use an IRES from HCV in the baculovirus vector containing a therapeutic gene. One would have been motivated to do so in order to receive the expected benefit, as suggested by Finkelstein et al and actually exemplified by Urabe et al, of obtaining more efficient expression of two cistrons separated by an IRES from HCV in a baculovirus vector system for treatment of a disease. Absent of any evidence to the contrary, there would have been reasonable expectation in using an HCV IRES because other have successfully used an IRES from HCV in therapeutic dicistronic viral vectors.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tara L Garvey whose telephone number is (571) 272-2917. The examiner can normally be reached on Monday through Friday 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that

the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tara L Garvey
Examiner
Art Unit 1636

TLG

JAMES KETTER
PRIMARY EXAMINER